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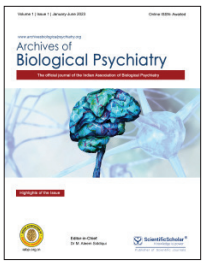

Case Report *Psychopharmacology*

A novel approach towards behavioral and psychological symptoms of dementia management

Eshani Pandey[1], Veena Tejan[1], Shobit Garg[1]

[1]Department of Psychiatry, SRI Guru Ram Rai Institute of Medical and Health Science, Dehradun, Uttarakhand, India.

***Corresponding author:**
Dr. Shobit Garg,
Department of Psychiatry,
SRI Guru Ram Rai Institute of Medical And Health Science,
Dehradun, India.

shobit.garg@gmail.com

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ABSTRACT

Dementia is the loss of cognitive functioning to the extent that it interferes with the person's daily routine functioning. Evidence suggests that there are millions of people living with dementia and this number is ever increasing as the younger age mortality is on the decline. The various causes of dementia can be diagnosed by a thorough medical history, a general and systemic examination, laboratory investigations, and neurological imaging. Although cognitive impairment is required and even sufficient for the diagnosis of dementia, the disease may also be accompanied by neuropsychiatric symptoms known as behavioral and psychological symptoms of dementia (BPSD), which are widespread and have a significant impact on the disease's prognosis and treatment. In this case report, we will be discussing about a novel approach undertaken when managing the BPSD symptoms of two patients older than 90 years of age. The patients were admitted to the inpatient department of a tertiary care hospital. The patients were started on low-dose medications initially but due to no improvement, a more rigorous approach had to be taken.

Keywords: Dementia, BPSD, Oldest-old patients, Management

INTRODUCTION

Dementia is characterized by cognitive impairment involving memory as well as at least 1 of the other domains, including personality, praxis, abstract thinking, executive functioning, language, complex attention, social, and visuospatial skills.[1]

For those at very advanced ages, the cases increase from 13%/year in the 90–94 age group, to 21%/year in the ages 95 to 99, and to 41%/year in ages beyond 100. Hence, it can be said that every 5.5 years, there is a doubling.[2,3] Although cognitive impairment is required and even sufficient for the diagnosis of dementia, this disease may also be accompanied by neuropsychiatric symptoms known as behavioral and psychological symptoms of dementia (BPSD), which are widespread and have a significant impact on the disease's prognosis and treatment.[3] These symptoms are varied and largely unpredictable in the patients, affecting their emotional experience, thought content, perception, and motor function.[4]

The clinical features of BPSD include a wide array of affective, psychotic, and behavioral signs and symptoms such as apathy, anxiety, depression, delusions, hallucinations, sexual or social disinhibition, disturbances in the sleep-wake cycle, aggression, agitation, and other behaviors which may be regarded as inappropriate.[5]

It is vital to identify and manage BPSD at the earliest, not just due to the disability caused to the patients, but because they are also known to heighten the caregiver burden.

In this article, "*the oldest old*" refers to people who are aged 90 years or older. A report published in 2011 by the US Census Bureau stated that the commonly used term of "oldest old" should be used for those people aged 90 and beyond.[6]

The diagnostic challenges and underlying neuropsychiatric symptoms of dementia are strikingly different in the 90 years and older population as compared to early-onset dementia.

Primarily first-line treatment for any BPSD is non-pharmacological. Various non-pharmacological strategies are reminiscence therapy, music therapy, validation therapy, simulated presence therapy, aromatherapy, acupuncture, light therapy, and cognitive rehabilitation. However, moderate-to-severe intensity BPSD including psychosis needs pharmacological intervention.[7] The pharmacological treatment consists of antipsychotics and other psychotropic agents such as antidepressants, mood stabilizers, and cognitive enhancers.[8]

A network meta-analysis comparing the efficacy and safety of atypical antipsychotics for the treatment of BPSD published in 2019 concluded that a single most effective and safe treatment option does not exist and clinicians should have an individualized approach when prescribing antipsychotic medications.[9]

Among antidepressants, tricyclic antidepressants are not recommended due to increased side effects. Among selective serotonin reuptake inhibitors (SSRIs), citalopram (not available in India) has shown efficacy in reducing agitation (CitAD trial),[10] but there are safety concerns as it may lead to QTc prolongation. Other antidepressants such as escitalopram, buspirone, and mirtazapine have been poorly studied[11] With all available evidence (not strong), citalopram and mirtazapine could be better choices as compared to other SSRIs in terms of managing agitation and associated lesser side effects.[12] At present, with the exception of carbamazepine, other mood stabilizers had little support of evidence. Other antiepileptic drugs such as gabapentin and pregabalin can be chosen for BPSD when carbamazepine cannot be given or tolerated by the patients.[13] According to a recent meta-analysis, a combination of an acetylcholinesterase inhibitor and memantine has shown superior efficacy over monotherapy.[14]

In this article, we will be reviewing two case vignettes of patients aged 96 and 94 years reporting BPSD, their clinical features, and their subsequent management.

CASE 1

A 96-year-old female, with a known case of hypertension for 30 years and on Tab Telmisartan 40 mg once daily (OD) for the same, presented to the psychiatry outpatient department with complaints of self-muttering, suspiciousness, on and off episodes of aggression, and decreased sleep for the past 15 days. The complaints were acute in onset, continuous, and progressively deteriorating in nature. About 15 days back, her family members first noticed that the patient when alone in her room started staying fearful unlike before. She started getting suspicious that there was someone trying to harm her and was even seen muttering to herself. Her complaints worsened during the evening and night, due to which she was unable to sleep. Furthermore, there were reports of irrelevant talks all night. She was admitted for the same. In addition, her family members also reported forgetfulness for 2 months wherein she would forget having taken her meals and medications. It would be difficult for her to button down her clothes properly or even remember the names and recognize the faces of her family members. Her magnetic resonance imaging (MRI) was suggestive of chronic ischemic changes and cortical atrophy. Her Montreal Cognitive Assessment score (MOCA) and Mini-Mental State Examination (MMSE) score were 8 and 10, neuropsychiatric inventory (NPI) score was 52. The frontal lobe assessment score was 6. Her Grasp reflex was present and palmomental reflex was present. Baseline investigations were sent which showed ESR raised to 26 mm/h, neutrophils raised to 76.8%, blood urea level was 25 mg/dL, uric acid level was 8.6 mg/dL, and sodium levels of 138 mmol/L. Her total cholesterol was raised to 280 mg/dL, Vit. D levels reduced to 32 Nmol/L, free T3 levels decreased to 4.05 pmol/L, and homocysteine levels raised to 35 mcmol/L. She was kept on a provisional diagnosis of major neurocognitive disorder. She was started at a dose of 10 mg Memantine OD along with Tab Rivastigmine at a dose of 1.5 mg OD and syrup Risperidone at a dose of 0.5 mL twice daily (BD) with syrup melatonin 3 mL at bedtime. Furthermore, 200 mg Valproate was added in syrup form at a dose of 5 mL OD and Tab clonidine 100 mcg 1 tab at bedtime. There was a significant improvement on this treatment regimen; hence, the same was continued. The patient was subsequently discharged from the hospital on the same treatment regimen with advice for weekly follow-up for the next 4 weeks and thereon a follow-up every 2 weeks for the next 4 weeks. The patient showed significant improvement on her second follow-up visit after 2 weeks wherein her NPI score dropped to 35 with improvement in the domains of aggression, irritability, and nighttime behavior disturbances with minimal side effects. However, her family members reported no improvement in complaints of forgetfulness and MOCA and MMSE scores were still poor showing a score of 8 and 12.

CASE 2

A 94-year-old female, with a known case of hypertension for 25 years, presented to the psychiatry outpatient department with complaints of irritability, suspiciousness, self-muttering, decreased sleep, and forgetfulness for 1 month. She was on

Tab Telmisartan 40 mg OD for hypertension. Her family members reported that the patient would get irritable over trivial things and started staying suspicious that her family members were on purpose making her take medicine, which she does not require, she would also often be seen muttering in audible words under her breath and when her family members would enquire, she would get irritable and start using abusive language toward them. She would also be seen wandering in the house during the night time reluctant to go to bed and on occasion would forget whether she has consumed her meals or not. Her baseline investigations were sent which showed a normal ESR level along with normal thyroid, renal, and liver function tests, and normal blood counts. Her total cholesterol was raised to 300 mg/dL, Vit. D levels reduced to 42 Nmol/L, and with normal homocysteine levels.

Her grasp reflex and palmomental test were positive and MMSE, MOCA, and NPI scores were 12, 10, and 48, respectively. Her MRI brain was suggestive of cerebral and cerebellar atrophy. She was kept on a provisional diagnosis of major neurocognitive disorder. She was started on Tab Clonidine 100 mcg 1 tab at bedtime, Syp Valproate 5 mL/200 mg, Syp Risperidone 0.5 mL BD, Tab Memantine 10 mg OD, and Syp Melatonin 5 mL at bedtime. The MRI brain was suggestive of cerebral and cerebellar atrophy. The patient showed improvement on the aforementioned treatment regimen when the patient was followed up after 2 weeks. Her NPI showed a decreased score of 32 with improvement in domains of irritability, delusion, and hallucinations. However, no improvement in complaints of forgetfulness was seen as the patient had difficulty recalling about having taken her medications or performing previously known tasks such as cooking and bathing properly. Her MOCA and MMSE scores showed no improvement resulting in the same score of 12 and 10.

DISCUSSION

Even in the oldest old, age remains an important risk factor for dementia. However, it appears that the impact of common risk factors for all types of dementia changes as people age, with some risk factors having inverse or diminished effects while others have an increased effect on the risk of developing dementia.[15]

For instance, both of our patients are known cases of hypertension, and evidence indicates that increased blood pressure is associated with an increased risk of dementia at ages under 74 years but is protective against dementia at ages over 85 years.[16]

Furthermore, aging also alters the pharmacokinetics and pharmacodynamics, and the oldest old age patients are particularly affected by these age-related changes and are in turn linked to more unfavorable outcomes.[17]

Although the treatment strategies are essentially the same for the oldest-old patients as they are for the younger elderly, there is however an invariable approach of "start low, go slow" that is particularly more important in this patient population of the oldest-old.[16]

Studies in the aspect of management of BPSD in the oldest old patients are minimal and the management stated in the ones that have been done talk about "start low, go slow" approach due to the risk of development of side effects. Keeping in mind these treatment approaches despite increased irritability and anger outburst in the patients, the patients were started on a low-dose antipsychotic and quetiapine. However, following no improvement, a more rigorous approach had to be undertaken. The patients were then started on an increased dose of a high potency antipsychotic; risperidone 1 mg, an antiepileptic/mood stabilizer sodium valproate 300 mg along with sympatholytic clonidine 100 mcg on which both the patients showed noteworthy improvement without any significant side effects. Clonidine is an antihypertensive medication that acts on alpha-adrenergic and imidazoline receptor agonists and it lowers blood pressure and heart rate by relaxing the arteries and increasing the blood supply to the heart.[18]

According to studies, there is diminished production of melatonin in dementia, and the role of melatonin in the restorative value of sleep (perceived sleep quality) and its sleep-anticipating effects resulting in attenuated activation of certain brain networks are gaining a new perspective as the role of poor sleep quality.[19]

Furthermore, studies suggest that melatonin also prevents atherosclerotic progression through the blockage of NLRP3 inflammasome activation and inflammatory factor secretion, which is a novel mechanism of melatonin against atherosclerosis.[20]

CONCLUSION

The present case report shows that a rigorous approach may be taken for the management of BPSD in the oldest old age patients without significant long-term side effects. However, the results seen in this case report are short term and for more concrete results, more trials of this treatment regimen are required in a larger number of patients.

Ethical committee

Approval from the Ethical Committee was obtained.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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